DETAILED ACTION

Response to Amendment

1. Applicant's amendment of claims 1, 7, 12 is acknowledged and has been entered.

2. Applicant's cancellation of claims 22 and 23 is acknowledged and has been entered.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 1-6, 10-12, 15, and 19-21 are rejected under 35 U.S.C. 102(e) as being anticipated by Monforte [US 7,091,046].

With respect to claim 1, Monforte teaches multiplexed assays for determining protein levels within a sample (column 2, lines 40-45), wherein the proteins are overexpressed within a host cell (column 21, lines 38-41). Monforte further discloses a binding moiety such as an antibody attached to a solid support that captures the target protein and a second binding moiety comprising a second antibody containing a signal generating element then binds to the captured target protein (column 13, lines 55-65), wherein both antibodies may act as affinity reagents. The bound protein is then detected and quantitated by optional amplicfication and expression of

predetermined marker components associated with the polypeptide binding components (column 14, lines 1-8).

5. With respect to claim 2, the proteins may be derived from a cell lysate or a blood sample (column 2, lines 59-64), or from organs (column 14, lines 60-65).

6. With respect to claim 3, Monforte further discloses a binding moiety such as an antibody attached to a solid support that captures the target protein (column 13, lines 55-65), wherein the antibodies may be monoclonal or polyclonal (column 17, lines 35-40).

7. With respect to claim 4, Monforte discloses that the antibodies may comprise IgG immunoglobulins (column 7, lines 42-50).

8. With respect to claim 5, the solid support may comprise a silicon chip (column 12, lines 65-67), to which biological molecules are linked or contacted (column 12, lines 51-56).

9. With respect to claim 6, Monforte discloses that mass spectrometry may be used for detecting the proteins (column 30, lines 38-41).

10. With respect to claims 10, 11, Monforte discloses substrates comprised of glass (column 12, lines 56-65), which is a chromatographic resin.

11. With respect to claim 12, Monforte discloses that the method may comprise binding target proteins to phage displayed antibodies, followed by a wash step to remove unbound components, and then the bound proteins are then eluted and used infect host cells, wherein the aggregated expression of the different target proteins is detected (column 16, lines 25-45)

12. With respect to claim 15, Monforte further discloses a binding moiety such as an antibody attached to a solid support that captures the target protein (column 13, lines 55-65).

13. With respect to claim 19, Monforte discloses that detection methods may include electrochemical detection and fluorescent detection (column 4, lines 1-14).

14. With respect to claim 20, Monforte teaches multiplexed assays for determining protein levels within a sample (column 2, lines 40-45), wherein the proteins are derived from one or more cells (column 2, lines 55-63). In particular, Monforte teaches using simple purifying method in order to prepare the samples for analysis (column 32, lines 45-39). Monforte further discloses the steps of providing a binding moiety such as an antibody attached to a solid support to captures the target protein and then applying a second binding moiety containing a signal generating element then binds to the captured target protein (column 13, lines 55-65). The protein is then detected and quantitated (column 14, lines 1-8). After detection, an analysis module is used for compiling the data into a database containing a profile for each sample or each target polypeptide in a sample (column 37, lines 20-25).

15. With respect to claim 21, Monforte discloses that the target proteins may comprise recombinant proteins (claim 2).

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. Claims 7-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Monforte [US 7,091,046] in view of Hutchens et al. [US 2001/0014461].

With respect to claim 7, Monforte teaches multiplexed assays for determining protein levels within a sample (column 2, lines 40-45), wherein the proteins are derived from one or more cells (column 2, lines 55-63). Monforte further discloses a binding moiety such as an antibody attached to a solid support that captures the target protein and a second binding moiety containing a signal generating element then binds to the captured target protein (column 13, lines 55-65). The protein is then detected and quantitated (column 14, lines 1-8) using methods such as matrix-assisted laser desorption/ionization (MALDI) time of flight mass spectrometry (column 4, lines 5-10). Monforte does not teach the use of surface enhanced laser desorption/ionization.

Hutchens et al., however, disclose that surface-enhanced laser desorption/ionization (SELDI) such as surface enhanced neat desorption (SEND) (para. 0190) represents a significant advance over MALDI in terms of specificity, selectivity, and sensitivity (para. 0188).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to adapt the method of Monforte to use detection methods such as SELDI and SEND, in order to achieve better specificity, selectivity, and sensitivity.

18. With respect to claim 8, Hutchens et al. disclose applying a layer of energy absorbing material (matrix material) onto which the analyte (the target proteins of Monforte) is placed which absorb the desorbing energy (from the laser) and cause the analyte to be desorbed (para. 0190).

19. With respect to claim 9, Hutchens et al. discloses a support for surface-enhanced laser desorption/ionization (SELDI), more specifically, for surface enhanced neat desorption (SEND) (para. 0190).

20. Claims 13 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Monforte [US 7,091,046] in view of Schwarz [Schwarz, Five-membered mercaptoheterocyclic ligands for thiophilic adsorption chromatography, 1996, J Mol Recog 9, 672-674].

With respect to claims 13 and 14, Monforte teaches antibodies attached to solid supports (column 13, lines 55-65), wherein the support comprises chromatographic resins such as glass (column 12, lines 56-65). Monforte fails to teach that the antibodies are attached by derivatizing the support with a capture molecule that binds to the antibodies, wherein the capture molecule is Protein A, Protein G, or a mercaptoheterocyclic ligand.

Schwarz, however, discloses that mercaptoheterocyclic ligands readily adsorb antibodies in a highly specific manner (p. 673, col.2, para. 3).

Therefore, one of ordinary skill in the art at the time of the invention would have been motivated to derivatize the support of Monforte, as taught by Schwarz, in order to ensure that the antibodies were properly attached to the support in a highly specific manner. This would thus prevent the likelihood of the antibodies from detaching from the support during the course of the assay, while also reducing the likelihood of nonspecific binding.

21. Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Monforte [US 7,091,046] in view of Piasio et al. [US 4,098,876].

With respect to claim 16, Monforte discloses a step wherein a binding moiety such as an antibody attached to a solid support captures the target protein and a second binding moiety comprising a second antibody with a signal-generating element then binds to the captured target

protein (column 13, lines 55-65). Monforte fails to teach the step of first binding the target proteins in the sample to the labeled antibody, and then binding with the immobilized antibody.

Piasio et al, however, teach first immobilizing the sample containing the target proteins with a labeled antibody and then a second incubation with the immobilized antibody (column 3, lines 14-25), and further discloses that this allows for a higher assay sensitivity to be achieved and eliminates the need for an intermediate washing step (column 3, lines 28-33).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to have first immobilizing the sample containing the target proteins with a labeled antibody and then a second incubation with the immobilized antibody in the method of Monforte, as suggested by Piasio et al., in order to obtain a higher assay sensitivity, and to reduce the complexity of the method by eliminating an intermediate washing step.

22. Claims 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Monforte [US 7,091,046] in view of Piasio et al. [US 4,098,876], as applied to claim 16 above, and further in view of Hutchens et al. [US 2001/0014461] and Schwarz [Schwarz, Five-membered mercaptoheterocyclic ligands for thiophilic adsorption chromatography, 1996, J Mol Recog 9, 672-674].

With respect to claims 17 and 18, Monforte teaches antibodies attached to solid supports (column 13, lines 55-65), wherein the support comprises chromatographic resins such as glass (column 12, lines 56-65). Monforte fails to teach that the immobilized antibodies are attached by derivatizing the support with a capture molecule, wherein the capture molecule is Protein A,

Protein G, or a mercaptoheterocyclic ligand. Monforte also fails to teach that the solid support is a surface enhanced laser desorption/ ionization biochip.

Hutchens et al., however, disclose that surface-enhanced laser desorption/ionization (SELDI) such as surface enhanced neat desorption (SEND) (para. 0190) represents a significant advance over MALDI in terms of specificity, selectivity, and sensitivity (para. 0188).

Schwarz further discloses that mercaptoheterocyclic ligands readily adsorb antibodies in a highly specific manner (p. 673, col.2, para. 3).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to adapt the method of Monforte to use detection methods such as SELDI and SEND, and utilize a surface enhanced laser desorption/ ionization biochip, in order to achieve better specificity, selectivity, and sensitivity.

One of ordinary skill in the art at the time of the invention would have further been motivated to derivatize the support of Monforte, as taught by Schwarz, in order to ensure that the immobilized antibodies were properly attached to the support in a highly specific manner. This would thus prevent the likelihood of the antibodies from detaching from the support during the course of the assay, while also reducing the likelihood of nonspecific binding.

Response to Arguments

23. Applicant's arguments filed January 22, 2008 have been fully considered but they are not persuasive.

24. With respect to applicant's argument that Monforte do not teach the detection of the captured host protein, but rather teach the detection of a detectable signal component, the Office notes that while Monforte does indeed teach the detection of a detectable signal component such

as a phage, but further specify that the purpose of this is for the detect the expression levels and physical attributes of tens to hundreds of proteins in a sample (column 14, lines 46-50). While the claims are read in light of the specification, limitations in the specification may not be read into the claims. Since applicant has not recited the steps by which the detection process occurs, the claim must be given its broadest reasonable interpretation which would read upon indirect means of detecting the captured host protein taught by Monforte.

25. Applicant's arguments with respect to the rejections under 35 U.S.C. 103(a) appear to rely in part on applicant's argument with respect to Monforte, which has been discussed above. It is noted that applicant merely recites a surface enhanced laser desorption/ionization biochip and applying a matrix material to the biochip, but never actually addresses on what molecules the SELDI process is performed on, such as the captured host proteins. Since, Hutchens et al. discloses a support for surface-enhanced laser desorption/ionization (SELDI), more specifically, for surface enhanced neat desorption (SEND) (para. 0190), and further provides motivation for using SELDI or SEND instead of MALDI as taught by Monforte, the rejection is proper.

26. With respect to applicant's arguments that using SELDI or SEND would unnecessarily complicate the detection of the amplified markers of Monforte, the Office notes that Hutchens et al. disclose that surface-enhanced laser desorption/ionization (SELDI) such as surface enhanced neat desorption (SEND) (para. 0190) represents a significant advance over MALDI in terms of specificity, selectivity, and sensitivity (para. 0188), which would motivate one of ordinary skill in the art to utilize SELDI or SEND instead of MALDI in the method of Monforte.

27. The Office notes that while it the invention taught by applicant may be different than that disclosed by Monforte, the claims as currently recited are broad enough to read upon the methods taught by Monforte. For these reasons, the rejections have been maintained.

Conclusion

28. No claims are allowed.

29. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

30. Any inquiry concerning this communication or earlier communications from the examiner should be directed to NELSON YANG whose telephone number is (571)272-0826. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571)272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

31. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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